UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/675,208	09/29/2000	Chieko Osumi	195378US0DIV	2452

22850 7590 12/19/2001

OBLON SPIVAK MCCLELLAND MAIER & NEUSTADT PC
FOURTH FLOOR
1755 JEFFERSON DAVIS HIGHWAY
ARLINGTON, VA 22202

EXAMINER	
BAUM, STUART F	7
ART UNIT	PAPER NUMBER
1638	

DATE MAILED: 12/19/2001

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/675,208	Applicant(s) OSUMI ET AL.	
	Examiner Stuart Baum	Art Unit 1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 13-36 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 13-36 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☒ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

The preliminary amendment file on December 19, 2000 has been entered. Claims 1-12 are cancelled and claims 13-36 are pending and are examined on the merits.

Acknowledgment is made of applicant's claim for foreign priority based on an application filed in Japan on April 26, 1996. It is noted, however, that applicant has not filed a certified copy of the Japanese application as required by 35 U.S.C. 119(b).

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper time wise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims13-36 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-5 of U.S. Patent No. 6166292 (listed in 1449).

Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims are obvious over the claims of Patent No. 6166292. Claims 1-5 are drawn to an isolated DNA which originates from an organism having an ability to produce raffinose from sucrose and galactinol, with the nucleotide sequence comprising at least nucleotide residues 57 to 2408 of the nucleotide sequence of SEQ ID NO:4 and encodes a protein which has the amino acid sequence of SEQ ID NO:5 exhibiting inherent properties of an isolated raffinose synthase protein as described in Patent No. 6166292 column 3 last paragraph. In addition, claim 25 of the present application which is drawn to an isolated DNA encoding a raffinose synthase is obvious over Patent No. 6166292 because it is described in said patent the procedure for preparing a DNA encoding a raffinose synthase from cucumber.

Claims 13-36 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 7, 8, and 10-12 of copending Application No. 09/425055. Although the conflicting claims are not identical, they are not patentably distinct from each other because claims 7, 8, and 10-2 are drawn to a DNA encoding a raffinose synthase comprising the nucleotide residues 56 to 2407 of SEQ ID NO:4 and a DNA encoding a protein specified by SEQ ID NO:5, exhibiting inherent properties of an isolated raffinose synthase protein which reads on the same material as specified in the claims of the present application.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> **The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.**

Claims 13-36 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicants clailm DNA encoding a raffinose synthase having specified biochemical properties, or that will hybridize to SEQ ID NO:4 or has homology with SEQ ID NO:4 or encodes a protein with homology to SEQ ID NO:5.

The inventors claim a nucleic acid sequence, SEQ ID NO: 4 referred to as raffinose synthase and a polypeptide sequence, SEQ ID NO: 5, derived from the former. Raffinose synthase catalyzes the formation of raffinose from galactinol and sucrose. The Applicants screened a cDNA library from cucumber and isolated DNA encoding raffinose synthase. The cDNA encoding raffinose synthase was subcloned into a vector in a sense and antisense orientation, operably linked to the 35S promoter. Said constructs were transformed into *Arabidopsis* and subsequent transformed plants were analyzed for raffinose content. In plants harboring either orientation of the isolated raffinose synthase encoding DNA, 0.0 mg/g raffinose were detected compared to wild type whose raffinose content was 0.2 mg/g. The Applicants

present three additional sequences SEQ ID NO's : 1, 2, and 3 which are short amino acid sequences taken from SEQ ID NO:5 which they state can be used to generate PCR primers.

The applicants do not identify structural features unique to a raffinose synthase protein that has the specified biochemical properties recited in claim 1, nor the functional domains of the protein. The Federal Circuit has recently clarified the application of the written description requirement to inventions in the field of biotechnology. See University of California v. Eli Lilly and Co., 119 F.3d 1559, 1568, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). In summary, the court stated that a written description of an invention requires a precise definition, one that defines the structural features of the chemical genus that distinguishes it from other chemical structures. A definition by function does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is. Given the lack of description for the cucumber raffinose synthase protein, it remains unclear what features identify a raffinose synthase protein, including a raffinose synthase gene with 35% homology to SEQ ID NO:4. Since a raffinose synthase protein has not been described by specific structural features, the specification fails to provide an adequate written description to support the generic claims.

Claims 13-36 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for claims limited to an isolated cucumber raffinose synthase gene of SEQ ID NO:4 encoding SEQ ID NO:5 does not reasonably provide enablement for claims broadly drawn to any polynucleotide encoding any protein with at least 35% similarity to SEQ ID NO:5 or any protein with 65% homology in the region in between the 510^{th} and 610^{th} amino acid of SEQ ID NO:5. The specification does not enable any person skilled in the art to which it

pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The claims are broadly drawn to nucleic acids encoding a plant raffinose synthase polypeptide including modifications of SEQ ID NO:4 which encodes SEQ ID NO:5. The instant specification, however, fails to provide guidance for which amino acids of SEQ ID NO:5 can be altered and to which other amino acids, and which amino acids must not be changed, to maintain activity of the encoded protein. The specification also fails to provide guidance for which amino acids can be deleted and which regions of the protein can tolerate insertions and still produce a functional enzyme.

It cannot be predicted by one of skill in the art that nucleic acids that have 35% to 99% homology will encode a protein with the same activity as the raffinose synthase protein. Bowie et al (1990, Science 247:1306-10) teach that an amino acid sequence encodes a message that determines the shape and function of a protein and that it is the ability of the protein to fold into unique three-dimensional structures that allows it to function and carry out the instructions of the genome. The cited reference also teaches that the prediction of protein structure from sequence data and, in turn, utilizing predicted structural determinations to ascertain functional aspects of the protein, is extremely complex (pg 1306, left column). Bowie et al teach that while it is known that many amino acid substitutions are possible in any given protein, the positions within the protein's sequence where such amino acid substitutions can be made with a reasonable expectation of maintaining function are limited. Certain positions in the sequence are critical to the three-dimensional structure/function relationship, and these regions can tolerate only conservative substitutions or none at all (pg 1306, right column). The sensitivity of proteins to

alterations in even a single amino acid in a sequence is exemplified by Burgess et al (1990, J. Cell Biol. 111:2129-2138), who teach that the replacement of a single lysine residue at position 118 of acidic fibroblast growth factor by glutamic acid led to a substantial loss of heparin binding, receptor binding, and biological activity of the protein.

Small changes in amino acid sequence can completely modify enzymatic function; Broun et al (1998, Science 282:1315-1317) teach that a change of four amino acids converts an oleate 12-desaturase to a hydroxylase. Thus, Broun et al demonstrated that one or few amino acid substitutions could dramatically affect the biological activity and the structure-function characteristics of a protein.

Hill et al (1998, Biochem. Biophys. Res. Comm. 244:573-577) teach when three histidines that are maintained in ADP-glucose pyrophosphorylase across several species are substituted with the "nonconservative" amino acid glutamine, there is little effect on enzyme activity, while the substitution of one of those histidines with the "conservative" amino acid arginine drastically reduced enzyme activity (see Table 1). All these mutated proteins, however, would have at least 95% identity to the original protein. The nucleic acids encoding all these mutated proteins, however, would hybridize under high stringency to the nucleic acids encoding the original protein.

Furthermore, the claims are broadly drawn to nucleic acids encoding a plant raffinose synthase polypeptide including modifications of SEQ ID NO:4 which encodes SEQ ID NO:5. However, the prior art teaches a protein with 35.1% homology (Heck et al 27 April, 1993 NCBI accession M77475.1) which is not a raffinose synthase. Given the existence of a protein that falls within the scope of the claim, which has a wholly different activity, the specification must

specify the functional domains of the enzyme that are required for proper activity and how one skilled in the art can assay putative proteins for raffinose synthase activity.

Given the unpredictability of determining the function of an isolated nucleic acid other than SEQ ID NO:4 on the basis of its nucleotide sequence alone and the unpredictability of finding a raffinose synthase gene that hybridizes to SEQ ID NO:4, or that encodes a protein having at least 35% identity to SEQ ID NO:5, for the reasons stated above; given the lack of working examples of raffinose synthase genes other than SEQ ID NO:4; given the absence of guidance with regard to identification of other raffinose synthase genes from the multitude of sequences that would hybridize to SEQ ID NO:4 or would encode a protein having at least 35% identity to SEQ ID NO:5, given the state of the prior art which does not provide further guidance about raffinose synthase genes; and given the breadth of the claims which encompass a multitude of sequences that have not been exemplified, it would require undue experimentation by one skilled in the art to make and/or use the claimed invention.

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stuart Baum whose telephone number is (703) 305-6997. The examiner can normally be reached on Monday-Friday 8:30AM – 5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Paula Hutzell can be reached on (703) 308-4310. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 305-3014 for regular communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Stuart Baum Ph.D.

December 14, 2001

ELIZABETH F. McELWAIN
PRIMARY EXAMINER
GROUP 1600